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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,348	07/17/2006	Allan L. Goldstein	2600-112	4572
6449 7590 10/16/2008 ROTHWELL, FIGG, ERNST & MANBECK, P.C. 1425 K STREET, N.W. SUITE 800 WASHINGTON, DC 20005				
EXAMINER NOAKES, SUZANNE MARIE				
ART UNIT		PAPER NUMBER		
1656				
NOTIFICATION DATE		DELIVERY MODE		
10/16/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

### Office Action Summary

**Application No.**

10/551,348

**Applicant(s)**

GOLDSTEIN, ALLAN L.

**Examiner**

SUZANNE M. NOAKES

**Art Unit**

1656

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4, 6-14 and 31 is/are pending in the application.
- 4a) Of the above claim(s) 10 and 11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-19, 12-14 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-8506)
- Paper No(s)/Mail Date 05/15/2008 and 10/01/2008
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Applicants are notified that the location and Examiner handling the instant Application has changed in the Office. Please note that all further correspondence should be sent to Art Unit 1656 and to the Examiner signed below.

### ***Status of the claims***

2. The amendments to the claims filed 19 June 2008 are acknowledged. Applicants have cancelled claims 5, 15-20 and 32. Claims 1-4, 6-14 and 31 are pending.
3. In an effort to clarify the record the following summarizes the status of claims thus far and attempts to clarify where the claims stand at the moment.

The previous Examiner had required restriction of SEQ ID NO: 1, 2 and 3, which was not an election of species, but rather an election of an entire Group (see Restriction Requirement 25 October 2007). Furthermore, an election of species was required for claims 4/20 and claim 8/24. In the response dated 19 November 2007, Applicants elected Group I (claims 1-14) and SEQ ID NO: 1 to be examined and additionally elected the species fibrin in claim 4 and thymosin  $\beta$  4 (T $\beta$ 4) in claim 8. Claims 8, 10 and 11 were subsequently withdrawn from consideration by the Examiner for Group I as being drawn non-elected subject matter.

It is noted that the restriction requirement between SEQ ID NO: 1, 2 and 3 is hereby withdrawn; SEQ ID NO: 1 (LKKTET), the elected sequence is encompassed entirely within SEQ ID NO: 2 (KLKKTET) and 3 (LKKTETQ). It is further noted that SEQ ID NO: 1, 2 and 3 are found within the polypeptide T $\beta$ 4 (a 43 amino acid peptide – see

instant specification, 1-2. paragraph 005 – wherein SEQ ID NO: 1 is amino acids 18-23; SEQ ID NO: 2 is amino acids 17-23 and SEQ ID NO: 3 is amino acids 18-24 of full length human T $\beta$ 4 (e.g. including the N-terminal Met) – see NCBI sequence information for NP\_066932).

Thus, claim 8 will be rejoined and examined with the elected claims. However, claim 1 now currently reads on the elected Group I AND the elected species of T $\beta$ 4 and there thus are no generic claims pending. Claims 10 and 11 remain withdrawn from consideration for being drawn to non-elected subject matter. The elected species of fibrin for claim 4 remains and fibrinogen, fibrin glue and collagen remain withdrawn.

4. Thus, claims 1-4, 6-9, 12-14 and 31 are subject to Examination on the merits.

#### ***Information Disclosure Statement***

5. The IDS filed 15 May 2008 has been received and is signed and considered, a copy of the PTO 1449 is attached to the following document.

#### ***Withdrawal of Previous Rejections***

6. Upon further consideration, the rejection of claims 1-7, 9 and 12-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

7. Upon further consideration, the rejection of claims 1-7, 9 and 12-14 and 31 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out

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and distinctly claim the subject matter which applicant regards as the invention.

Thymosin  $\beta$  is a well known protein in the art.

8. The rejection of claims 1-3, 9, 12-14 and 31 under 35 U.S.C. 102(b) as being anticipated by WO 00/06190 is withdrawn. Applicants correctly point out that said reference does not teach an adhesive.

9. In view of the amendments to the claims, the rejection of claims 1-7, 9, 12-14 and 31 under 35 U.S.C. 103(a) as being unpatentable over WO 00/06190 and Schryver et al., US Publication No. 2003/0055511 is withdrawn because the composition is not taught as being obvious to covalently attach the individual components (e.g. and adhesive and a polypeptide such as SEQ ID NO: 1 or thymosin  $\beta$ ) is covalently bound together.

### ***New Rejections/Objections***

#### ***Claim Rejections - 35 USC § 101***

10. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 6-9, 12-14 and 31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to compositions comprising a covalently bound adhesive (such as fibrin) and a polypeptide of SEQ ID NO: 1, 2 or 3 or thymosin $\beta$ 4. With respect to said sequences, it is noted that each of SEQ ID NO: 1, 2 and 3 are found within the full length polypeptide T $\beta$ 4 (a 43 amino acid peptide – see instant specification, 1-2.

paragraph 005 – wherein SEQ ID NO: 1 is amino acids 18-23; SEQ ID NO: 2 is amino acids 17-23 and SEQ ID NO: 3 is amino acids 18-24 of full length human T $\beta$ 4 (e.g. including the N-terminal Met) – see NCBI sequence information for NP\_066932).

Huff et al. (FASEB Journal, 2002 May;16(7):691-6) teach that thymosin $\beta$ 4 can be covalently cross-linked to proteins such as fibrin and collagen *naturally* by tissue transglutaminase (meets claims 1-4, 6, 8, 31). It is noted that after activation of human platelets with thrombin, thymosin $\beta$ 4 is released and crosslinked to fibrin (meets claim 4) in a time- and calcium-dependent manner and the covalent cross-linking of the T $\beta$ 4 and fibrin or collagen is mediated by factor XIIIa (meets claim 5), a transglutaminase that is coreleased from stimulated platelets. This provides a mechanism to increase the local concentration of thymosin $\beta$ 4 near sites of clots and tissue damage, where it may contribute to wound healing, angiogenesis and inflammatory responses (meets claim 2) [see Huff et al., Abstract and Discussion, pp. 694-695, especially Scheme 1).

With regard to the limitation of claim 9 and that the polypeptide is recombinant or synthetic, it is noted that all naturally occurring is recombinant and recombines to produce said polypeptides.

Thus the claimed composition is a naturally occurring composition and there is nothing about the instant claimed invention that shows the hand of man and thus it constitutes non-statutory subject matter.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1-4, 6-9, 12-14 and 31 are also rejected under 35 U.S.C. 102(a) as being anticipated by Huff et al.

The teachings of Huff et al. are recited above. It is further noted that while the composition is a naturally occurring one as disclosed above, Huff et al. also teach the composition in isolation. Specifically isolated T $\beta$ 4 was covalently cross-linked to fibrin or fibrinogen or collagen or actin (see Figures 1-3, and p. 693, 1<sup>st</sup> column, last paragraph to 2<sup>nd</sup> column, 1<sup>st</sup> paragraph) and the covalent cross-linking of the two catalyzed by isolated transglutaminase (Factor XIIIa).

The concentrations of fibrin to T $\beta$ 4 was 0.2U to 0.04 mg/ml which meets the molar ratios of claims 12-14.

An additional experiment was performed with isolated human thrombocytes and was a composition wherein T $\beta$ 4 was covalently cross-linked to fibrin by naturally occurring Factor XIIIa which was naturally present in the composition (see p. 693, 2<sup>nd</sup> column, last two paragraphs). Furthermore, one skilled in the art would expect the cross-linking to occur for any form of T $\beta$ 4 as well.

***Response to Arguments***

13. Applicant's arguments, filed 19 June 2008, with respect to the previous Office action have been considered. All of the previous rejections of record have been withdrawn for the reasons recited in Sections 4-7 of the instant Office action.

***Conclusion***

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Suzanne M. Noakes/  
Examiner, Art Unit 1656  
30 September 2008